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The evidence of Kv4.2 internalization in response to NMDAR activation as presented by the authors is clear, persuasive, and exciting. The contribution of this novel process to LTP is sure to excite additional work in order to iron out differences between the present study and previous work. For example, Frick et al. (2004) used on-cell patch recording to study dendritic I_A before and after LTP induction in ex vivo hippocampal slices. They reported that the voltage dependence of channel inactivation was altered slightly, reducing channel availability, but they did not report any evidence consistent with internalization. Clathrin-mediated endocytosis is thought to underlie internalization of AMPARs in long-term depression (Man et al., 2000). It will be a challenge to determine how the cell sorts its plasma membrane proteins after LTP induction so that Kv4.2 channels are internalized, but not AMPARs. Finally, it will be interesting to determine whether depotentiation restores I_A and spine Kv4.2 channels. If not, then the authors' hypothesis makes a clear prediction that depotentiation should be greater at −80 mV than at −60 mV. There is nothing like an exciting result and a good controversy to send the LTP crowd rushing to their rigs!

An often neglected finding is that strong correlated activity not only potentiates excitatory synaptic transmission itself, but it also results in a potentiation of the ability of a given amount of synaptic excitation to induce action potentials in the postsynaptic cell (Andersen et al., 1980). Like the synaptic component of LTP, this phenomenon, known as potentiation of excitation-spike coupling, is NMDAR dependent, input specific, and bidirectional (Daoudal et al., 2002). The internalization of Kv4.2 and decrease in I_A described by Kim et al. would seem to be consistent with descriptions of changes in EPSPs after LTP (Abraham et al., 1987) and therefore offers an attractive explanation for potentiation of excitation-spike coupling. Kim et al. have shown us that I_A is in play—let the follow-up experiments begin!

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Finding Our Way around the Sensory-Motor Corner

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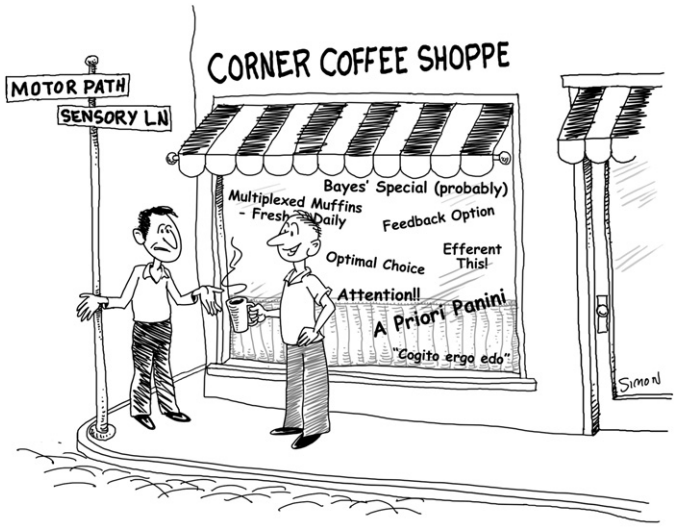
DOI 10.1016/j.neuron.2007.06.012

Our understanding of how sensory information is transformed into motor commands has grown increasingly sophisticated. In this issue of *Neuron*, Wilmer and Nakayama use a novel analysis to show that the initial changes in smooth-pursuit eye speed are driven by low-level motion signals, whereas the later eye speed is determined by high-level signals.

Conventional wisdom once held that sensory-motor processing for saccadic and pursuit eye movements might be explained by a relatively straightforward pair of transformations. On the one hand, saccades involve transforming signals about the locations of stimuli into the bursts of motor activity needed to quickly redirect the eyes toward these stimuli. On the other hand, pursuit eye movements are generated by a different set of transformations that convert signals about visual motion into the motor commands that smoothly rotate the eyes. Although these types of transformations are still viewed as fundamental steps in turning the sensory-motor corner for eye movements, the overall process is considerably more complicated (see Figure 1). The pursuit and saccadic systems do not operate independently, but instead they interact with each other and are also linked to



"Sure I like the new menu, but I really miss the Bode plots."

Figure 1. Recent Research Has Revealed Increasingly Complex Processes Associated with Sensory-Motor Transformations

higher-order processes like visual attention (Krauzlis, 2005). Moreover, the sensory signals themselves are a heterogeneous collection (Derrington et al., 2004), reflecting the diverse processing capabilities of the visual system.

In this issue of *Neuron*, Wilmer and Nakayama (2007) reveal another surprising facet to this story. They provide evidence that different parts of pursuit eye movements are driven by very different types of visual motion signals. The earliest part of pursuit—the change in eye speed that occurs before the catch-up saccade that typically accompanies pursuit—is determined by "low-level" signals, which compute speed directly from the luminance changes in the retinal image. The later part of pursuit—the steadier eye speed that occurs after the saccade—is determined by "high-level" signals, which first identify salient features in the image and then track those features over time.

Establishing these relationships involves a clever combination of psychophysics, eye movement recordings, statistics, and, critically, an unusually large pool of experimental subjects (45 college students). First, each subject was run on a pair of perceptual tests to measure the precision of their low-level and high-level speed judgments. For the low-level test, subjects were tested with luminance gratings that drifted too rapidly to be judged by the position of the gratings' bars. For the high-level test, there were no moving luminance edges, and instead, the sense of motion depended on tracking changes in the contrast of the stimulus. Importantly, the perceptual performance of the subjects varied widely but was statistically independent between the two tasks.

Second, the same subjects were tested on a pursuit eye movement task, which simply involved using the eyes to follow a dot that moved in one of the cardinal directions at one of several speeds. Two primary measures of the subjects' motor performance were extracted from these eye movement responses: the change in eye speed prior to the catch-up saccade (presaccadic acceleration) and the degree to which eye speed matched target speed after the catch-up saccade (postsaccadic precision).

Finally, exploiting the statistical power of their large subject pool, Wilmer and Nakayama (2007) tested the correlation across subjects between perceptual performance on the two speed judgment tasks and motor performance on the pursuit eye movement task. Two striking associations emerged from this analysis. Subjects that were more precise in their perceptual judgments of low-level motion tended to show higher presaccadic eye acceleration during pursuit. Conversely, subjects that were more precise in their judgments of high-level motion tended to show greater postsaccadic precision during pursuit. On the other hand, performance on the low-level task was not related to postsaccadic precision, nor was performance on the high-level task related to presaccadic eye acceleration.

These results provide compelling evidence that different types of visual motion signals contribute to different aspects of the pursuit motor output. Implicit in the experimental design is the idea that the same visual motion signals that drive pursuit eye movements also support visual perception. This idea has a long history (Steinbach, 1976), but it is not without controversy because it violates another popular idea that there are separate visual pathways for action and perception (Goodale and Milner, 1992). At least for visual motion and eye movements, the weight of recent evidence tilts in favor of a common stage of processing (Stone and Krauzlis, 2003; Osborne et al., 2005), and the current findings nicely demonstrate that this principle applies to both high- and low-level systems of visual motion processing.

One interpretation of these findings is that the changes in the quality of pursuit are primarily determined by changes in the visual motion signals available to the motor system. For example, the computation of object motion takes some time, and both pursuit and perception initially respond based on local image motion and only later follow the global motion of the object (Masson and Stone, 2002; Pack and Born, 2001). However, there are limits to this interpretation. The motor system is not a passive conduit for visual signals, but plays an active role in shaping the descending signals into the eye motor commands. For example, they add a boost to the final motor command to compensate for the lagging dynamics of the ocular periphery. Thus, the switch from low-level to high-level motion signals might be due, at least in part, to the

selective and strategic use of different descending signals during different phases of pursuit motor control (e.g., low-level signals may be more effective at driving the initial acceleration).

Perhaps the most striking finding in the study is that the catch-up saccade itself, rather than just the passage of time during the trial, appears to be critical for the emergence of the association between high-level speed judgments and the precision of post-saccadic pursuit. Moreover, a control experiment presented in the supplementary material shows that when the catch-up saccade is eliminated, the association disappears. These findings are puzzling, because other experiments have found that saccades are not necessary for smooth-pursuit of high-level motion. For example, when viewing a display containing bidirectional apparent motion, subjects experience reversals in perceived motion that can be smoothly followed with reversals in pursuit eye velocity without making any saccades (Madelain and Krauzlis, 2003).

One possibility is that saccades, pursuit, and high-level position tracking are all supported by common estimates of target position. Given that the time course of these estimates would likely vary from trial to trial, the occurrence of the targeting saccade would provide a temporal marker for when the estimate had reached a critical level, and pursuit would be expected to show changes at around the same time. This explanation also predicts that the effects observed by the authors should not be restricted to pursuit but apply to the saccades themselves. For example, subjects that were more precise in their judgments of high-level motion would be expected to show greater precision in the endpoints of their saccades. Presumably, estimates of target position remain available even when saccades are not executed, but without the temporal marker provided by saccades, the effects may become too diffuse to detect.

As these results illustrate, the sensory-motor corner provides a unique window into some of the core issues in systems neuroscience. Most likely, there are other surprising findings in store.

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Autophagy Induction Rescues Toxicity Mediated by Proteasome Inhibition

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DOI 10.1016/j.neuron.2007.06.005

The ubiquitin-proteasome and macroautophagy-lysosome pathways are major routes for intracytosolic protein degradation. In many systems, proteasome inhibition is toxic. A *Nature* article by Pandey et al. shows that this toxicity can be modulated by altering autophagic activity. Their tantalizing results suggest that overexpression of *HDAC6* may increase flux through the autophagy pathway, thereby attenuating the toxicity resulting from proteasome inhibition.

Intracytosolic proteins can be degraded either by the ubiquitin-proteasome system or by a range of lysosome-related pathways (reviewed in Rubinsztein, 2006). The ubiquitin-proteasome pathway typically regulates levels of short-lived proteins. These are usually initially tagged for degradation by linkage of a ladder of ubiquitin molecules to lysine residues. The ubiquitin chain constitutes a recognition sequence that allows them to be transported to the proteasome, a barrel-shaped, multiprotein, proteolytic complex. The proteasome degrades the proteins into peptides, which are further degraded to amino acids by cytosolic and nuclear peptidases.

The proteasome has a narrow pore, which precludes entrance of organelles, multiprotein complexes, and